Pigmented Nevi

Induced Changes in the Junctional Component

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■ *The pigmented nevus represents a potentially more dynamic lesion than has been indicated by most published studies. New nevus cell clusters frequently appear in the epidermis over the residual portion of a nevus that remains after partial surgical excision. Even in relatively inactive nevi in adults, new junctional nevus cells may be induced by surgical trauma. This stimulated growth usually regresses by the time one year or more has elapsed. The growth of nevus cells is probably comparable to that induced in other cells by traumatic injury. There is no evidence to suggest that it is related to the development of melanoma in pigmented nevi.*

PIGMENTED NEVI may grow during the course of their development. During the growing period one usually finds nevus cells in the epidermis as junctional foci, so-called because of their location at the dermal-epidermal junction. These intra-epidermal cells are commonly viewed as an expression of growth activity, but the identification of multiplication of these cells is difficult.

Several reports have indicated that new epidermal nevus cell foci may appear after surgical planing or other excision of the surface of certain nevi.[3,5,6,7,8] Most of these lesions have been in children and with one exception[6] those where a preliminary histological study was made have presented junctional foci at the time of the initial operation. Our investigations[2] have indicated that junctional activity may be induced commonly, even in intradermal nevi, as a sequel to superficial partial surgical excision followed by light electrodesiccation.

This finding was derived from the examination of 143 intradermal or compound nevi from 103 patients, 85 of whom were beyond the age of 20. The superficially excised portion was examined histologically and the lesions were divided into three classes on the basis of the character of the junctional component. Class 1 represented the intradermal nevi, including those with occasional small epidermal foci of the sort that can be found in many intradermal nevi on serial sectioning.[4] Class 2 and Class 3 exhibited moderate and marked junctional activity respectively. Subsequent biopsy specimens from the same lesions were removed from one month to six years later. Forty-four showed only scar tissue, leaving 99 residual nevi, which were compared with the corresponding initial biopsy specimens.

The study showed that the regenerated epidermis over the residual intradermal portion of partly excised nevi frequently contained nevus cells in clusters duplicating those of the intra-epidermal portion of untreated compound nevi (Figure 1). In some lesions this represented a return of a junctional component, often in an exaggerated form, following partial excision of an initially compound nevus. In 34 instances there was a development of prominent intra-epidermal changes when the original lesion had been classed as an essentially intradermal nevus. (Figure 2). In most of these cases re-biopsy was done within 12 months after the partial excision (Table 1). In this group 68 per cent of the lesions that originally were Class 1 had become lesions of Class 2 or Class 3. Although the entire covering epidermis had been removed from the lesions which were initially Class 2 and Class 3, each of these, upon re-biopsy within one year, showed a regrowth of epidermal nevus cells, and the lesions remained as compound nevi.

The earliest reformation of intra-epidermal nevus

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Presented before the Section on Dermatology and Syphilology at the 94th Annual Session of the California Medical Association, San Francisco, 28 to 31 March 1965.

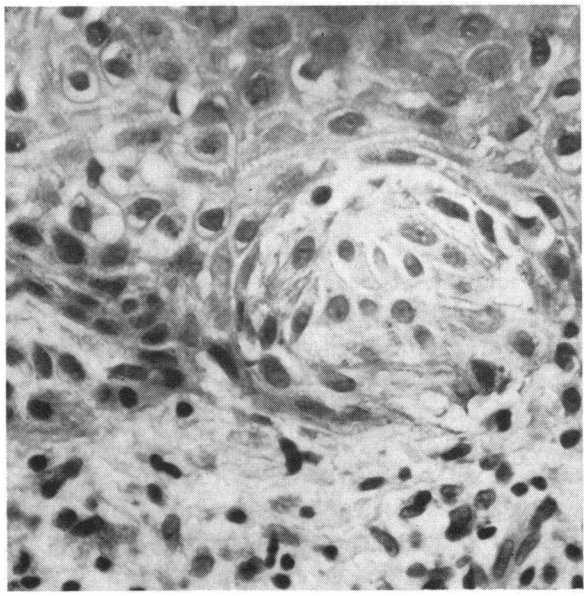

Figure 1.—Pigmented nevus cell cluster in regenerated epidermis three months after partial surgical excision of a nevus that showed no junctional activity in the initial specimen (Hematoxylin and eosin stain×600).

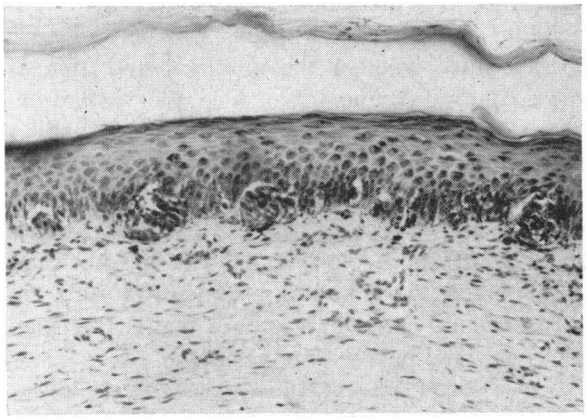

Figure 2.—Many small intra-epidermal nevus cell clusters and heavy pigmentation of the basal epidermal cells present one month after partial excision of a nevus that was initially intradermal. A prominent scar separates the newly formed junctional component from the dermal residue, which is not included in the photograph (Hematoxylin and eosin stain×140).

cells was seen in two specimens removed one month following the initial surgery. Similar induction of new intra-epidermal nevus cells, which were frequently more prominent than those of the initial specimens, occurred in five lesions after six weeks, and in 12 lesions after two months.

When the excision of nevus residues was carried out more than one year after the initial operation, however, a different situation was encountered (Table 2). Here approximately three-fourths of the persistent lesions showed inconspicuous junctional activity, and only one instance of marked intra-epidermal nevus cell growth was observed. In the latter case the second biopsy was performed only thirteen and a half months after the initial partial excision.

TABLE 1.—*Junctional Change Over Residual Nevi After Partial Surgical Excision (Lesions Studied Within One Year)*

Status at Original Biopsy	*Number of Lesions*	*Status at Second Biopsy (Per Cent of Lesions)*		
		Class 1	*Class 2*	*Class 3*
Class 1	41	32%	44%	24%
Class 2	17	....	71%	29%
Class 3	6	....	33%	67%

For definition of classes, see text.

These findings indicate that junctional activity in a nevus may be induced by appropriate means but that this growth is usually transient. Whether stimuli other than surgical trauma may evoke similar growth in nevi has not been tested, but the possibility is apparent that the natural history of some intact nevi may include episodes of increased growth of the epidermal component even after the structure of an intradermal nevus has been attained.

Discussion

These observations have not identified with certainty the source of the induced epidermal nevus cells. Although the great majority of such cells had been removed with the initial biopsy specimen, it is possible that a few residual foci in the surrounding epidermis or in remaining hair follicles served as the source of new nevus cells in the repaired epidermis. One cannot exclude entirely the suggestion of Schreus[7] that dermal nevus cells grew into the newly formed epidermis, particularly since a role of residual intradermal nevus cells appears to be an important aspect of the process which led to the appearance of junctional activity over residual nevi.

With three exceptions, intradermal nevus cells were always found whenever intra-epidermal nevus cells appeared in re-biopsy specimens. In two of the exceptions the specimen for study was sufficiently thin so that it may not have reached deeplying residual nevus cells. The dermal nevus remnant was frequently separated from the epidermis,

TABLE 2.—*Junctional Change Over Residual Nevi After Partial Surgical Excision (Lesions Studied After More Than One Year)*

Status at Original Biopsy	*Number of Lesions*	*Status at Second Biopsy (Per Cent of Lesions)*		
		Class 1	*Class 2*	*Class 3*
Class 1	24	75%	25%	....
Class 2	7	86%	....	14%
Class 3	4	25%	75%	....

For definition of classes, see text.

however, by a layer of scar tissue up to 1 mm thick, and there was no morphological evidence of migration of nevus cells from the residual dermal component. A final possibility is that the new nevus cells were derived from melanocytes in the regenerated epidermis. This would imply some special stimulatory mechanism, presumably related to the intradermal nevus cells.

Regardless of the origin of the new intra-epidermal nevus cells, it should not be surprising that they proliferated after trauma. Epidermal cells are often stimulated to rapid growth by trauma, and melanocytes have been shown to proliferate in association with regenerating epidermis.[1] If the nevus cells or their precursors possess any growth capacity comparable to that of melanocytes, this might be expected to be exaggerated as part of the active growth of all epidermal elements during repair.

Although the nature of the apparent influence of the dermal nevus remnant upon the induction of junctional nevus cell proliferation remains undetermined, the findings under discussion emphasize the relationship between the epidermal and dermal portions of nevi and speak against any basic qualitative differences between the common types of pigmented nevi.

An important question is whether traumatic stimulation of epidermal nevus cell growth relates in any way to the development of melanoma. There is no more reason *a priori* to believe that this should be the case than to expect squamous cell carcinoma to form in the regenerating epidermis over a wound. A great deal has been written, however, about the possibility of malignant transformation of nevi by trauma, and conflicting opinions have evolved. Our belief, supported by the absence of histological evidence of malignant change in any of more than 200 biopsy specimens obtained at different intervals following partial excision of nevi, is that surgical trauma does not induce melanoma. We have been unable to find any reported instance of melanoma that appeared at the site of a partially excised nevus after the removed portion had been found free from melanoma by adequate histological examination. Although we do not regard partial excision of benign nevi as dangerous, we emphasize the importance of histological examination of the excised portion of such nevi to insure that the lesions are indeed benign.

Another question relative to this study is whether recognition of the phenomenon of epidermal nevus cell regrowth has practical value. While its principal value is its contribution to understanding of the nature of pigmented nevi, appreciation of the nature of the stimulated junctional activity and its course may aid in the management of cases after partial excision of nevi. Local pigmentation appears frequently at the site of partially excised nevi, and this may be a source of worry unless it is recognized that, like the frequently associated regrowth of epidermal nevus cells, post-traumatic local pigment deposition in the basal layer of the epidermis over residual nevi appears early and decreases with the passage of time. In about half of the residual nevi which we have examined within one year, histological sections have shown more pigment in the regenerated epidermis than in that over the original lesion. After more than one year, however, only 9 per cent retained such increased epidermal pigment. This suggests that there is no cause for alarm if the skin over a partially excised nevus becomes prominently pigmented.

More extensive observations will be necessary to determine whether the ultimate regression of the epidermal component of nevi after partial excision is as great as that in untreated nevi, but since 88 per cent of the nevi in our series that were examined more than one year after partial excision had no recognizably greater junctional activity than was manifest in the original nevus, it seems highly probable that after several years the difference in junctional activity between treated and untreated nevi will be negligible.

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